

Remarks

Claims 1-24 are currently pending. The amendments made herein and cancellation of claims 2, 20, and 23 are made without prejudice to the filing of continuing applications.

Applicants have amended claims 1, 12, 17, 19, and 21. Claim 24 is new. No new matter is added by the amendments made herein.

Claim 1 has been amended to address the rejections based on prior art and 35 U.S.C. §112 second paragraph. Claims 12 and 17 have been amended to address 35 U.S.C §112 second paragraph rejections and Claims 19 and 21 have been amended to properly depend from amended claim 1. Applicants have made various amendments merely to improve the readability of the claims. None of these latter amendments has been made to address patentability.

Applicants note that the Office Action mailed January 09, 2006 confirms Applicants' election of Group I. The Restriction Requirement mailed September 22, 2005, placed claim 20 in Group III. However, the Action lists claims 1 and 3-21 as the invention of Group I. Thus, claim 20 appears to be improperly placed into Group I in the Action. Applicants consider claim 20 as being canceled since it is within non-elected Group III. Applicants respectfully requests clarification if they have misunderstood the the Office's position..

Claim 22 is withdrawn and Applicants respectfully request rejoinder of claim 22 pending allowance of claims 1, 3-19, and 21.

1. Rejections based on 35 U.S.C. § 112, second paragraph

Claims 1, 3-18, and 20 stand rejected as being indefinite under 35 U.S.C. §112, second paragraph.

Claims 1, 3-18, and 20 stand rejected as being indefinite because the Office considers the phrase "groups which are independently selected from halogen," on page 178, lines 2-3, to be confusing. In response, Applicants have removed the phrase and amended "halogen" to "halogens."

Claims 1, 3-18, and 20 stand rejected as being indefinite because the Office considers the phrase "(IV)-(CR_{C-x}RC-y)₀₋₄-heteroaryl," on page 181, lines 6-7, to be confusing. In response, Applicants have removed the phrase.

Claims 1, 3-18, and 20 stand rejected as being indefinite because the terms "R₁-aryl" and "R₁-heteroaryl," on page 180, lines 20 and 22, were not defined. In response, Applicants have amended the terms to "aryl" and "heteroaryl." Support for the amendments can be found at pages 167-169, page 195 lines 19-22, page 191 line 31, page 192 line 12, and page 193 lines 22-30.

Claims 12 and 17 stand rejected as being indefinite because the substituents as written were considered to be confusing. In

response, Applicants have amended claims 12 and 17 to clarify which groups are substituted.

Applicants submit that the claims, as amended, meet the requirements of 35 U.S.C. §112, second paragraph, and respectfully request reconsideration and withdrawal of the §112 rejections.

2. Rejection based on 35 U.S.C. § 102(e)

Claims 1 and 3-21 stand rejected under §102(e) as being anticipated by Fobian et al., WO 2004022523. Applicants note that the priority date for the instant invention, November 27, 2002, precedes Fobian's international filing date of September 08, 2003. The Office has not asserted that the subject matter of the pending claims is disclosed in the priority document for Fobian et al. Accordingly, since Applicants' priority application, which does describe the subject matter of the instant claims, predates the filing date of Fobian et al., the instant claims are not anticipated by the reference.

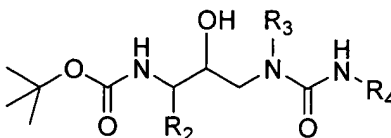
Claims 1 and 3-21 stand rejected under §102(e) as being anticipated by Birkus et al., WO 2003090691. Applicants note that the priority date for the instant invention, November 27, 2002, precedes the Birkus international filing date of April 25, 2003. The Office has not asserted that the subject matter of

the pending claims is disclosed in the priority document for Birkus et al. Accordingly, since Applicants' priority application, which does describe the subject matter of the instant claims, predates the filing date of Birkus et al., the instant claims are not anticipated by the reference.

3. Rejection based on 35 U.S.C. § 102(a)

Claims 1 and 3-21 stand rejected under §102(a) as being anticipated by John et al., WO 2003040096. Applicants note that the instant invention's priority date of November 27, 2002 precedes the John reference's publication date of May 15, 2003. Applicant respectfully submits that the John et al. reference is not prior art under 35 U.S.C. § 102(a).

Claims 1 and 3-21 stand rejected under §102(a) as being anticipated by Wolfe et al., WO 2002014264. Wolfe discloses examples of carbamates of general formula

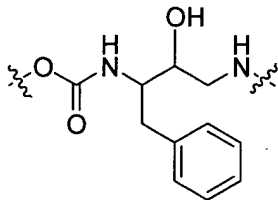


As amended, the claims do not encompass the carbamates disclosed in Wolfe. Specifically, variables $R_N-T-X-N(R_{20})-$ do not encompass carbamates and therefore the amended claims are not anticipated by Wolfe.

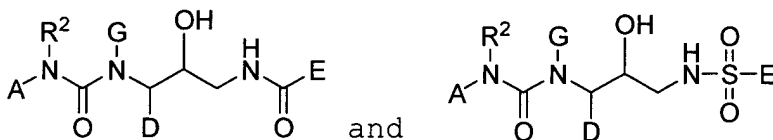
4. Rejection based on 35 U.S.C. § 102(b)

Claims 1 and 3-21 stand rejected under §102(b) as being anticipated by Hale et al., WO 2000047551.

Hale discloses examples of carbamates of general formula

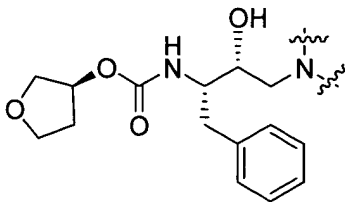


The claims in Hale encompass ureas of general formula



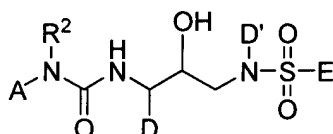
As amended, the claims do not encompass the carbamates disclosed in Hale. Also, the amended claims, as originally filed, do not encompass the ureas disclosed in Hale because R_c or R_{20} cannot form $-NH-C(=O)-E$ or $-NH-S(=O)_2-E$. Therefore, the amended claims overcome Hale.

Claims 1 and 3-21 stand rejected under §102(b) as being anticipated by Kamijo et al., JP 09124629. Kamijo discloses carbamates of general formula



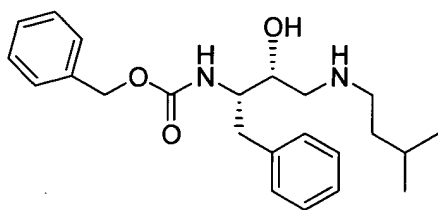
As amended, the claims do not encompass carbamates disclosed in Kamijo. Specifically, variables R_N -T-X-N(R_{20})- do not encompass carbamates and therefore the amended claims overcome Kamijo.

Claims 1 and 3-21 stand rejected under § 102(b) as being anticipated by Tung et al., WO 9633187. Tung encompasses ureas of general formula

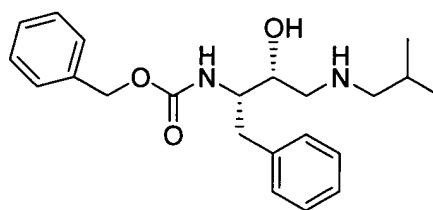


The claims, as originally filed, do not encompass the ureas disclosed in Tung because R_C or R_{20} cannot form N(D')-S(O)₂-E. Tung, therefore, does not anticipate the claims as originally filed or as amended.

Claims 1 and 3-21 stand rejected under 102(b) as being anticipated by Vazquez et al., US 5,578,606. Vazquez discloses compounds identified as examples 1 and 3 shown below:



Example 1



Example 3

These compounds are carbamates. As amended, the claims do not encompass the carbamates disclosed in Vazquez. Specifically, variables R_N -T-X-N(R_{20})- do not encompass carbamates because T

cannot be oxygen and therefore the amended claims overcome Vazquez.

5. Rejection based on 35 U.S.C. § 103(a)

Claims 1, 3-21 stand rejected as being obvious over Vazquez et al., J. Med. Chem. (1995), Vol. 38(4), pages 581-584, and all prior art references cited in the Office Action mailed January 9, 2006. As explained below, Tung did not render the original claims obvious and the amendments to the claims overcome Fobian, Birkus, John, Wolfe, Hale, Kamijo, and Vazquez.

The Supreme Court in Graham v. John Deere, 383 U.S. 1, 17, 86 S.Ct. 684, 694 (1966) set out the factual inquiry which the various district courts and the Patent Office must follow in determining obviousness. The Supreme Court's mandate was as follows:

"[u]nder .103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances."

Moreover, references cannot be combined absent some teaching, suggestion, or incentives supporting the combination. In re Geiger, 815 F.2d 686, 2 USPQ 2d 1276 (Fed. Cir., 1987). To properly combine two references to reach a conclusion of

obviousness, there must be some teaching, suggestion or inference in either or both of the references, or knowledge generally available to one of ordinary skill in the art which would have lead one to combine relevant teaching of the two references. Ashland Oil Inc. v. Delta Resins and Refractories, Inc., et al., 776 F.2d 281, 227 USPQ 657; 5 USPQ 2d 1532 (Fed. Cir., 1985). Both the suggestion to make the claimed composition or device or carry out the claimed process and the reasonable expectation of success must be found in the prior art, not in the applicants' disclosure. In re Vaeck, 20 USPQ 2d 1438 (Fed. Cir., 1991). The references cited by the examiner in this case do not render applicants' claims obvious since there is no suggestion in those references to combine their respective teachings; further, the requisite reasonable expectation of success cannot be found in the references.

Disqualification of Commonly Owned References Under 103(c)

Section 103(c) provides that subject matter developed by another person, which qualifies as prior art under 102(e) shall not preclude patentability under 103 where the subject matter and claimed invention were, at the time the claimed invention was made, owned by the same person.

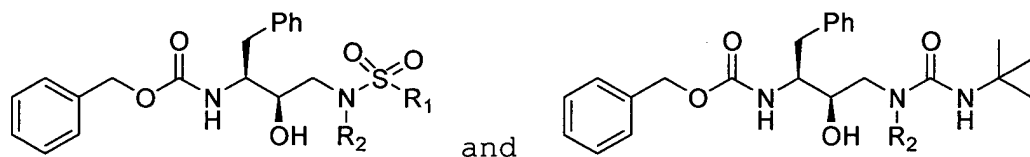
The instant application and WO 2004022523 (Fobian et al.) were, at the time the invention claimed herein was made, jointly owned by Elan Pharmaceuticals and Pharmacia UpJohn.

The instant application and WO 2003040096 (John et al.) were, at the time the invention claimed herein was made, jointly owned by Elan Pharmaceuticals and Pharmacia UpJohn.

Applicant respectfully submit that the Fobian et al. and John et al. references are disqualified as prior art under 103(c).

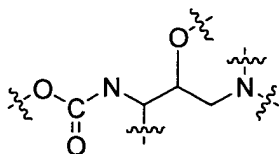
Scope and content of the Prior Art

Vazquez (J. Med. Chem.) discloses carbamates of general formulae



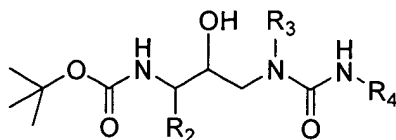
as inhibitors of HIV-1 Protease.

Birkus discloses carbamates of general formula



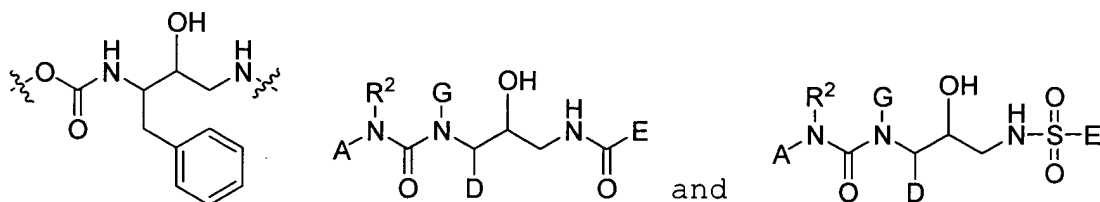
which are useful in anti-HIV therapy.

Wolfe discloses carbamates of general formula



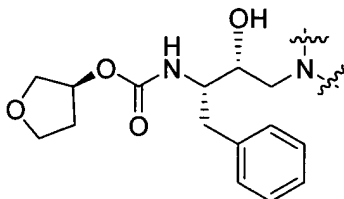
as inhibitors of certain aspartyl proteases involved in generating beta-amyloid from amyloid precursor protein.

Hale discloses compounds of general formula



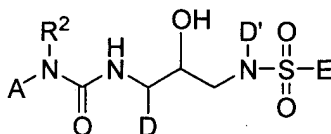
as HIV aspartyl protease inhibitors.

Kamijo discloses carbamates of general formula



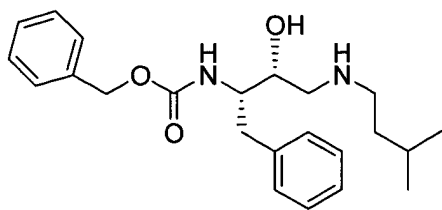
useful for preparing HIV protease inhibitors.

Tung discloses compounds of general formula

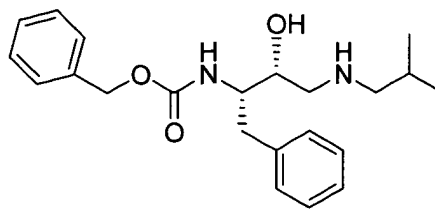


as HIV-1 and HIV-2 protease inhibitors.

Vazquez (US 5,578,606) discloses examples 1 and 3



Example 1

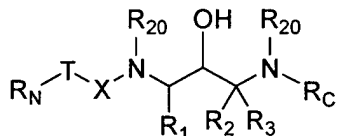


Example 3

as intermediates useful in the preparation of HIV protease inhibitors.

The Differences Between the Prior Art and the Claims

Vazquez (J.Med.Chem.) discloses compounds of general structure carbamate-C-C(OH)-C-sulfonamide and carbamate-C-C(OH)-C-urea. As amended, the claims of the instant application have formula



wherein T is N(R₂₀) and X is -(C=O)-, -(C=S)-, or -(C=N-Z)-. Carbamates are not encompassed by variables R_N-T-X-N(R₂₀)- and sulfonamides and ureas are not encompassed by variables N(R₂₀)-R_C as required by Vazquez (J.Med.Chem.).

Birkus discloses compounds of general structure carbamate-C-C(OH)-C-sulfonamide wherein the compounds are substituted with phosphonate ester groups. As noted above, carbamates are not encompassed by variables R_N-T-X-N(R₂₀)- and sulfonamides are not encompassed by variables -N(R₂₀)-R_C as

required by Birkus. Additionally, compounds of the instant invention cannot be substituted with phosphonate ester groups as required in Birkus.

Wolfe discloses compounds of general structure carbamate-C-C(OH)-C-urea. As noted above, carbamates are not encompassed by $R_N-T-X-N(R_{20})-$ and ureas are not encompassed by $-N(R_{20})-R_C$ as required in Wolfe.

Hale discloses compounds of general structure carbamate-C-C(OH)-C-sulfonamide and carbamate-C-C(OH)-C-amide. As noted above, carbamates are not encompassed by $R_N-T-X-N(R_{20})-$ and sulfonamides and amides are not encompassed by $-N(R_{20})-R_C$ as required in Hale.

Kamijo discloses compounds of general structure carbamate-C-C(OH)-C-sulfonamide and carbamate-C-C(OH)-C-alkyl. As noted above, $R_N-T-X-N(R_{20})-$ cannot encompass carbamates and sulfonamides are not encompassed by $-N(R_{20})-R_C$ as required by Kamijo.

Tung discloses compounds of general structure urea-C-C(OH)-C-sulfonamide. As noted above, sulfonamides are not encompassed by $-N(R_{20})-R_C$ as required by Tung.

Vazquez (US 5,578,606) discloses carbamates. As noted above, carbamates are not encompassed by $R_N-T-X-N(R_{20})-$ as required by Vazquez (US 5,578,606).

Level of Ordinary Skill in the Pertinent Art

All of Birkus, Wolfe, Hale, Kamijo, Tung and Vazquez were of at least ordinary skill in the art and the claimed invention did not occur to them.

Applicants respectfully submit that claims 1, 3-19, and 21 are not obvious in view of Vazquez (J.Med.Chem.). There is no motivation in Vazquez (J.Med.Chem.) to modify the reference compounds to result in the instantly claimed compounds. Vazquez (J.Med.Chem.) lists eleven carbamate-C-C(OH)-C-sulfonamide compounds in Table 1. One of skill in the art would conclude that the carbamate group and the sulfonamide group are necessary for the activity desired in Vazquez. Vazquez neither suggests nor motivates one of skill in the art to modify the reference compounds by 1) replacing the carbamate groups with urea groups and 2) removing the sulfonamide groups.

Birkus discloses several carbamate-C-C(OH)-C-sulfonamides substituted with phosphonate groups. One of skill in the art would conclude that the carbamate, sulfonamide, and, in particular, phosphonate groups are important to the activity desired in Birkus. One of skill in the art would not have been motivated by Birkus to modify the compounds disclosed therein by 1) replacing the carbamate groups with urea groups, 2) removing the sulfonamide groups, and 3) removing the phosphonate groups.

Wolfe discloses carbamate-C-C(OH)-C-ureas wherein peptides are attached to the urea. One of skill in the art would conclude that the carbamate and urea-peptide groups, situated on opposite ends of the isopropyl backbone, are necessary to the activity desired by Wolfe. One of skill in the art would not have been motivated to modify Wolfe's compounds by 1) replacing the carbamate groups with urea groups and 2) removing the urea-peptide groups.

Hale and Tung disclose urea-C-C(OH)-C-amides and urea-C-C(OH)-C-sulfonamides. One of skill in the art would conclude that the urea, sulfonamide, and amide groups of these references are important to the activities desired by Hale and Tung. There is nothing in either of these references, or other prior art, that would have motivated one of ordinary skill in the art to remove the sulfonamide or amide groups required by Hale and Tung.

Kamijo discloses carbamate-C-C(OH)-C-sulfonamides and carbamate-C-C(OH)-C-(isobutyl) compounds as synthetic intermediates useful in large scale preparation of HIV inhibitors. One of skill in the art would conclude that the carbamate groups are important components in the syntheses disclosed in the reference. Consequently, one of skill in the art would not have been motivated to remove the carbamate groups required by Kamijo. Further, nothing in this reference suggests

the modifications required to arrive at the claimed compounds. In other words, the carbamates of Kamiyo do not suggest the claimed ureas.

As shown above, Vazquez (US 5,578,606) discloses two carbamate-C-C(OH)-C-(alkyl) compounds. There is nothing in Vazquez (US 5,578,606) that amounts to a suggestion to replace the carbamate groups disclosed therein with urea groups as required in the instant claims. Thus, nothing in this reference suggests the modifications required to arrive at the claimed compounds.

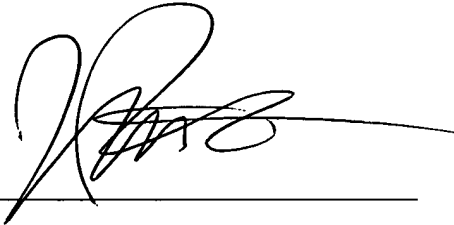
Applicants respectfully submit that the claims as amended are not rendered obvious by the cited references and request reconsideration and withdrawal of the §103(a) rejection.

Conclusion

Applicants respectfully submit that the amended claims meet all requirements of patentability. Allowance of the amended claims and passage of the case to issue are therefore respectfully solicited.

Should the Examiner believe a discussion of this matter would be helpful, he is invited to telephone the undersigned at (312) 913-2136.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'S. Sarussi', written over a horizontal line.

Dated: April 10, 2006

By:

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